

Phase II study of eribulin in combination with gemcitabine for the treatment of patients with locally advanced or metastatic triple negative breast cancer (ERIGE Trial). Clinical and pharmacogenetic results on behalf of the Gruppo Oncologico Italiano di Ricerca Clinica (GOIRC)

Musolino A, Cavanna L, Boggiani D, Zamagni C, Frassoldati A, Caldara A, Rocca A, Gori S, Piacentini F, Berardi R, Brandes AA, Foglietta J, Villa F, Pellegrino B, Todeschini R, Tognetto M, Naldi N, Bortesi B, Boni L, Montemurro F, Ardizzoni A Medical Oncology Unit and Gruppo Oncologico di Ricerca Clinica (GOIRC), University Hospital of Parma, Parma, Italy; Hospital of Piacenza, Piacenza, Italy; SSD Oncologia Medica Addarii, Bologna, Italy; Oncologia Clinica, Azienda Ospedaliero Universitaria di Ferrara, Ferrara, Italy; Oncologia Medica, Ospedale Santa Chiara, Trento, Italy; IRST-IRCCS, Meldola, Italy; Sacro Cuore-Don Calabria Hospital, Negrar, Italy; University Hospital of Modena, Modena, Italy; Ancona University Hospital, Ancona, Italy; Azienda USL-IRCCS, Bologna, Italy; Hospital of Perugia, Perugia, Italy; Lecco Hospital, Lecco, Italy; GOIRC, Parma, Italy; Careggi University Hospital, ITT, Firenze, Italy; Istituto per la Ricerca e la Cura del Cancro, IRCCS, Candiolo, Italy; Medical Oncology Unit, Policlinico S.Orsola-Malpighi, Bologna, Italy

**Background:** There are no well-established chemotherapy regimens for metastatic triple negative breast cancer. The combination of a microtubule inhibitor (eribulin) with a nucleoside analog (gemcitabine) may synergistically induce tumor cell death, especially in tumors like triple negative breast cancers (TNBC) characterized by high cell proliferation, aggressive tumor behavior, and chemo-resistance.

**Materials and Methods:** This is an open-label, national multicenter phase II study evaluating the combination of eribulin (0.88 mg/m<sup>2</sup>) plus gemcitabine (1000 mg/m<sup>2</sup>) on day 1 and 8, q21 as either first- or second-line treatment of locally advanced or metastatic TNBC. The primary endpoint was the objective response rate (ORR) for evaluable patients (pts). The study was designed according to the Simon's two stage optimal design. We chose the lower activity (p<sub>0</sub>) of 0.20 and target activity level (p<sub>1</sub>) of 0.35. A prospective, molecular correlative study has been being carried out on germinal DNA of study population to assess the role of BRCA mutations and single nucleotide polymorphisms (SNPs) in predicting efficacy and toxicity of the combination regimen.

**Results:** From July 2013 to September 2016, 83 evaluable pts (37 in the first stage, 46 in the second one) were enrolled. They received a median number of 6 cycles of treatment (range 1-24). The ORR (CR+PR) was 37.35% (90% CI: 28.47-46.93) and the clinical benefit rate (CR+PR+SD ≥ 24wks) was 48.78% (90% CI: 39.24%-58.39%). The most common grade 3-4 adverse events (> 10% of patients) were neutropenia and liver toxicity. With a median follow-up of 28.8 months, the median progression-free survival (PFS) and overall survival (OS) were 5.1 months (95% CI: 4.2-7.0) and 14.7 months (95% CI: 10.2-20.0), respectively. BRCA1/2 deleterious mutations were observed in 15 (22%) out of 68 genotyped pts. Women with BRCA1/2 mutations were associated with worse ORR, PFS and OS than those with BRCA1/2 wild-type. A panel of SNPs in genes of study drug metabolism pathways was evaluated. Among these, CYP3A4 392A >G and FGD4 2044236G >A SNPs were associated with greater liver toxicity by logistic regression analysis. Furthermore, CDA\*2 79A >C, RRM1 2455 A >G, and CYP2C8 416G >A SNPs were associated with poorer overall survival by Cox proportional hazards model.

**Conclusions:** The combination of eribulin and gemcitabine shows promising activity and a moderate toxicity profile in metastatic TNBC. BRCA status and pharmacogenetics tests may help identify pts with high probability of response with negligible toxicity.

Session: Poster Session 1: Treatment: Advanced chemotherapy (5:00 PM-7:00 PM)Date/Time: Wednesday,  
December 5, 2018 - 5:00 pm

Room: Hall 1